Short Communication

Immunotherapy in Cancer

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The immune system is a powerful weapon against disease, infections and defective cells. Because cancer cells are the body's mutated cells, they are not always recognized by the immune system as invaders. Also, cancer cells have multiple ways to evade, shut down or overpower an immune attack. Immunotherapy is the treatment that uses certain parts of a person's immune system to fight cancer.

What is the relationship between cancer and the immune system?

While many of our cells grow and divide naturally, this behavior is tightly controlled by a variety of factors, including the genes within cells. When no more growth is needed, cells are told to stop growing.

Unfortunately, cancer cells acquire defects that cause them to ignore these stop signals, and they grow out of control. Because cancer cells grow and behave in abnormal ways, this can make them stand out to the immune system, which can recognize and eliminate cancer cells through a process called *immunosurveillance*.

However, this process isn't always successful. Sometimes cancer cells develop ways to evade and escape the immune system, which allows them to continue to grow and metastasize, or spread to other organs. Therefore, immunotherapies are designed to boost or enhance the cancer-fighting capabilities of immune cells and tip the scales in the immune system's favor.

How does immunotherapy work against cancer?

This can be done in a couple of ways:

1. Boosting, the natural defenses of your immune system so it works harder to find and attack cancer cells.

2. Removing the block in the immune system that is preventing the immune system from attacking the cancer cell.

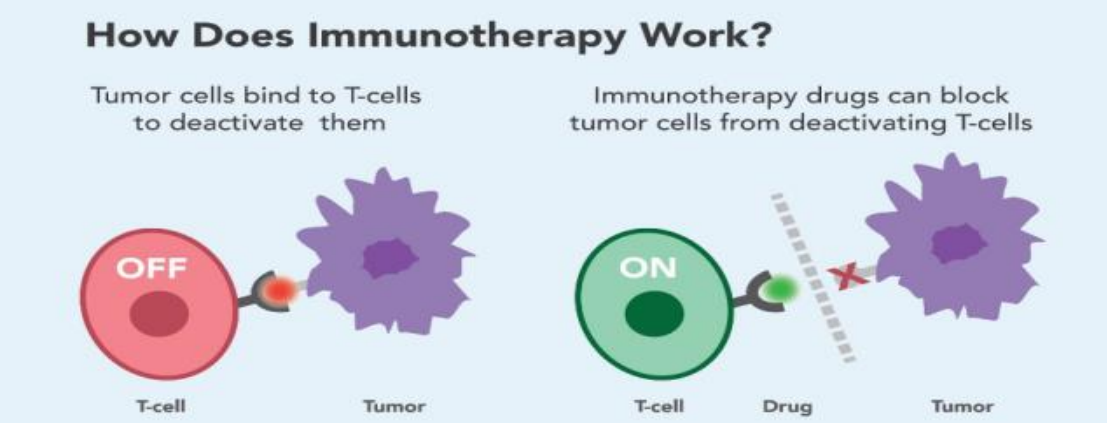

Figure 1

What is the difference between immunotherapy and chemotherapy?

Chemotherapy is a direct form of attack on rapidly dividing cancer cells, but this can affect other rapidly dividing cells including normal cells. When patients respond, the treatment's effects happen immediately. These direct effects of chemotherapy, however, last only as long as treatment continues.

Immunotherapy treats the patient's immune system, activating a stronger immune response or teaching the immune system how to recognize and destroy cancer cells. Immunotherapy may take more time to effect, but those effects can persist long after treatment ceases.

What types of immunotherapy treatments are there?

Immunotherapy treatments can be broken down into five types:

1. **Targeted antibodies** are proteins produced by the immune system that can be customized to target specific markers (known as antigens) on cancer cells, to disrupt cancerous activity, especially unrestrained growth. Some targeted antibody-based immunotherapies, known as antibody-drug conjugates (ADCs), are equipped with anti-cancer drugs that they can deliver to tumors. Others, called bi-specific T cell-engaging antibodies (BiTEs), bind both cancer cells and T cells to help the immune system respond more quickly and effectively.

2. **Adoptive cell therapy** takes a patient's immune cells, expands or otherwise modifies them, and then reintroduces them to the patient, where they can seek out and eliminate cancer cells. In CAR T cell therapy, cancer-fighting T cells are modified and equipped with specialized cancer-targeting receptors known as CARs (chimeric antigen receptors) that enable superior anti-cancer activity. Natural killer cells (NKs) and tumor-infiltrating lymphocytes (TILs) can also be enhanced and reinfused in patients.

3. **Oncolytic virus therapy** uses viruses that are often, but not always, modified to infect tumor cells and cause them to self-destruct. This can attract the attention of immune cells to eliminate the main tumor and potentially other tumors throughout the body.

4. **Cancer vaccines** are designed to elicit an immune response against tumor-specific or tumor-associated antigens, encouraging the immune system to attack cancer cells bearing these antigens. Cancer vaccines can be made from a variety of components, including cells, proteins, DNA, viruses, bacteria, and small molecules. Some versions are engineered to produce immune-stimulating molecules. Preventive cancer vaccines inoculate individuals against cancer-causing viruses and bacteria, such as HPV or hepatitis B.

5. Immunomodulators govern the activity of other elements of the immune system to unleash new or enhance existing immune responses against cancer. Some, known as antagonists, work by blocking pathways that suppress immune cells. Others, known as agonists, work by stimulating pathways that activate immune cells.

a. **Checkpoint inhibitors** target the molecules on either immune or cancer cells that tell them when to start or stop attacking a cancer cell.
b. **Cytokines** are messenger molecules that regulate maturation, growth, and responsiveness. Interferons (IFN) are a type of cytokine that disrupts the division of cancer cells and slows tumor growth. Interleukins (IL) are cytokines that help immune cells grow and divide more quickly.

Which cancers are treated with immunotherapy?

Immunotherapy drugs have been approved to treat many types of cancer including lung cancer, skin cancer (melanoma), urinary bladder cancer, kidney cancer, colon cancer, liver cancer (HCC), head and neck cancer, etc.

What are the side effects of immunotherapy?

Immunotherapy can cause side effects, many of which happen when the immune system that has been revved up to act against cancer also acts against healthy cells and tissues in your body. Fatigue is among the most common side effects seen, with an estimated overall frequency of 16 to 24 percent for the anti-programmed cell death receptor 1 (PD-1) and anti-programmed cell death ligand 1 (PD-L1) agents. Other common side effects include skin and mucosal toxicity, diarrhea and colitis, pneumonitis, hepatotoxicity and endocrinopathies. These side-effects don't occur immediately after initiation of immunotherapy, most of these are delayed side-effects. It is important to note that most of these side effects are reversible with appropriate interventions.

How can we tell whether immunotherapy is working?

Immunotherapy treatments may take longer to produce detectable signs of tumor shrinkage compared to traditional treatments. Sometimes tumors may appear to grow on scans before getting smaller, but this apparent swelling may be caused by immune cells infiltrating and attacking cancer. Many patients who experience this phenomenon, known as pseudoprogression, often report feeling better overall. In certain cancer types, immune-related side effects may be linked with treatment success.

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